Application of lung microphysiological systems to COVID-19 modeling and drug discovery: a review.

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Public Summary:
There is a pressing need for effective therapeutics for coronavirus disease 2019 (COVID-19), the respiratory disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus. The process of drug development is a costly and meticulously paced process, where progress is often hindered by the failure of initially promising leads. To aid this challenge, in vitro human microphysiological systems need to be refined and adapted for mechanistic studies and drug screening, thereby saving valuable time and resources during a pandemic crisis. The SARS-CoV-2 virus attacks the lung, an organ where the unique three-dimensional (3D) structure of its functional units is critical for proper respiratory function. The in vitro lung models essentially recapitulate the distinct tissue structure and the dynamic mechanical and biological interactions between different cell types. Current model systems include Transwell, organoid and organ-on-a-chip or microphysiological systems (MPSs). We review models that have direct relevance toward modeling the pathology of COVID-19, including the processes of inflammation, edema, coagulation, as well as lung immune function. We also consider the practical issues that may influence the design and fabrication of MPS. The role of lung MPS is addressed in the context of multi-organ models, and it is discussed how high-throughput screening and artificial intelligence can be integrated with lung MPS to accelerate drug development for COVID-19 and other infectious diseases.

Scientific Abstract:
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